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Rate of Synthesis of Coagulation Factors II, VII, IX, and X During Substitution Therapy with P.P.S.B.

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P.P.S.B., which I had been told by Dr. Soulier is now commercially available in sufficient amounts to be used on a large scale, appeared most suitable and convenient for the treatment of haemophilia B [1, 2]. Shortages of factors II, VII, and X, with the exception of acquired factor II-deficiency in lupus erythematosus and acquired factor X-deficiency in amyloidosis, should also respond well to P.P.S.B. Plasma levels of coagulation factors to be expected from the amount of P.P.S.B. transfused can be calculated by means of formulas used earlier [1]. It is evident that the levels obtained in a patient are proportional to the amount and to the biological t½ of the coagulation factors transfused. Once equilibrium between infusion rate and metabolic decay is attained in a patient displaying no production of his own, the requirement for maintenance of a 25% level would, per kg/hour, amount to the equivalent of fresh normal plasma for:

Factor II-deficiency	0.2 ml
Factor VII-deficiency	2.4 ml
Factor IX-deficiency	0.6 ml
Factor X-deficiency	0.36 ml

These amounts hold for normal metabolic conditions, under which the t½ of factors II, VII, IX, and X are 72, 6, 24 and 40 h respectively.

What we were not sure about until recently, but nevertheless appeared all important to know from the point of view of economy of substitution therapy, was whether the rate of the patient's own synthesis of the coagulation factors under discussion was altered during substitution. If the rate of synthesis were *not* altered, then the level obtained during transfusion of P.P.S.B. would be the sum of the patient's own level and the level to be expected from the amount transfused. Mild cases of factors II, VII, IX, and X deficiency, that is to say cases displaying a coagulation factor activity of 5%–20% of the missing coagulation factor, would then require substantially less P.P.S.B. for the attainment of the safe 25%–30% level.

We recently had an opportunity to study a haemophilia B patient belonging to the mild variety who was operated upon under the protection of P.P.S.B. The preparation was given at a constant infusion rate and the daily amount was equivalent to about 1.5 l fresh normal plasma (factor II 1.36 l, factor VII 1.52 l, factor IX 0.8 l, and factor X 1.48 l). Pertinent coagulation factor activities in the patient's plasma were measured twice daily during the whole period of substitution. Equilibrium between the infusion rate and rate of metabolic decay of the coagulation factors

Table I

	Coagulation factor activity (%)	
	calculated	measured
Factor II	218	183
Factor VII	84	103
Factor IX	40	41
Factor X	170	213

transfused was supposed to have been attained within the first four days of treatment, the plasma levels assessed between the 5th and 9th day being rather constant. Independence of production rate with respect to plasma levels is strongly suggested by the results obtained in this patient: as shown in table I, the plasma levels measured for factors II, VII, IX, and X appeared to be in reasonable accordance with the sum of patient's basic levels (basic levels: 96%, 72%, 16%, and 95% resp.) and the level calculated from the amount transfused (calculated levels: 122%, 12%, 24%, and 75% resp.). All figures given in table I are average values of 8 observations.

In conclusion: Our statement, made some years ago, that patients suffering from mild coagulation disorders in case of major trauma or major surgery should with respect to substitution be regarded as severely affected, seems likely to be wrong, since transfusion of large amounts of factors II, VII, IX, and X into a patient suffering from mild haemophilia B did not diminish the rate of synthesis of these factors. Hence, adequate substitution, i.e. attainment and maintenance of a 25%–30% level, will be easier to obtain in mild deficiency of factors II, VII, IX, and X than in cases of severe deficiency of these coagulation factors.

References

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